

07/22/02 1130 U.S. PTO

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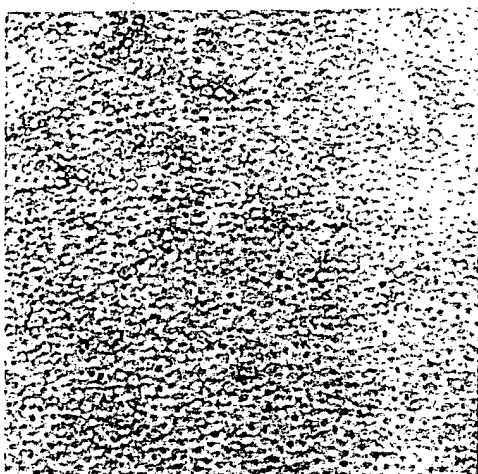


FIG. 1A

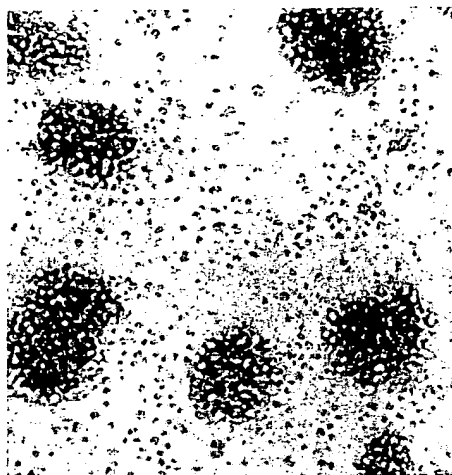


FIG. 1B

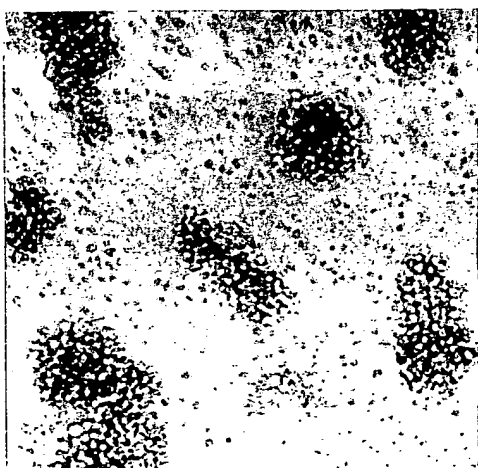


FIG. 1C

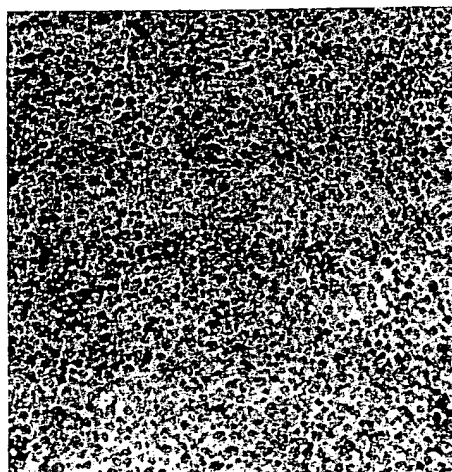
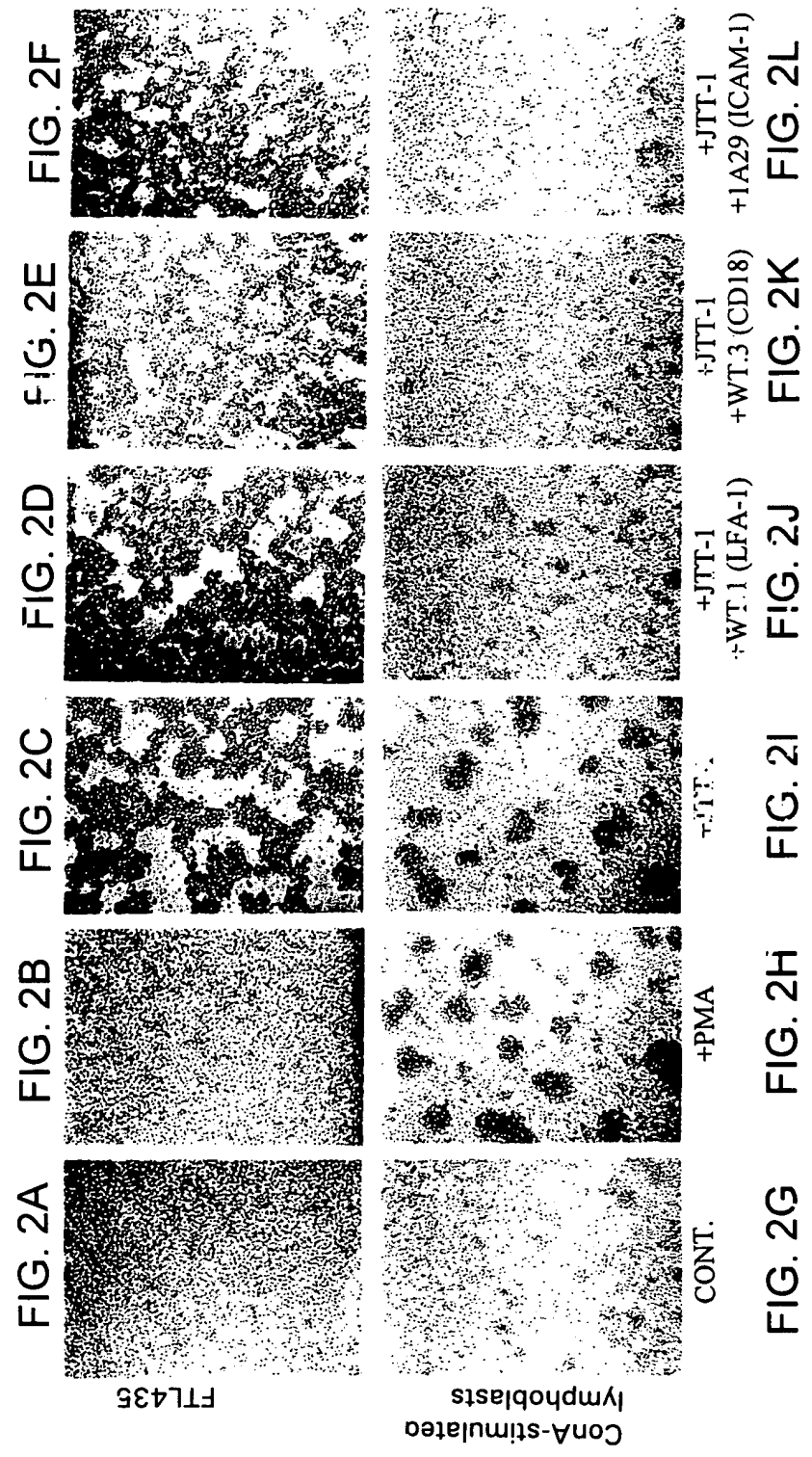


FIG. 1D

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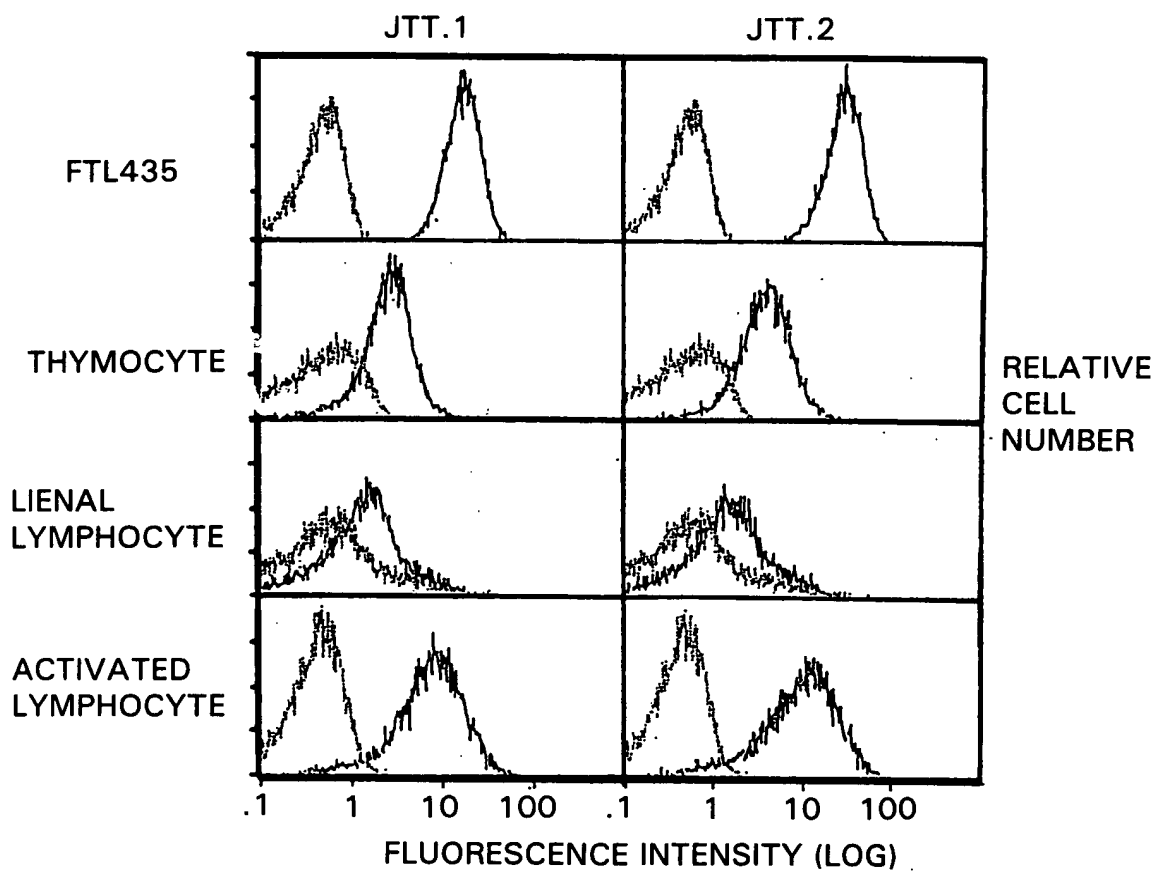


FIG. 3

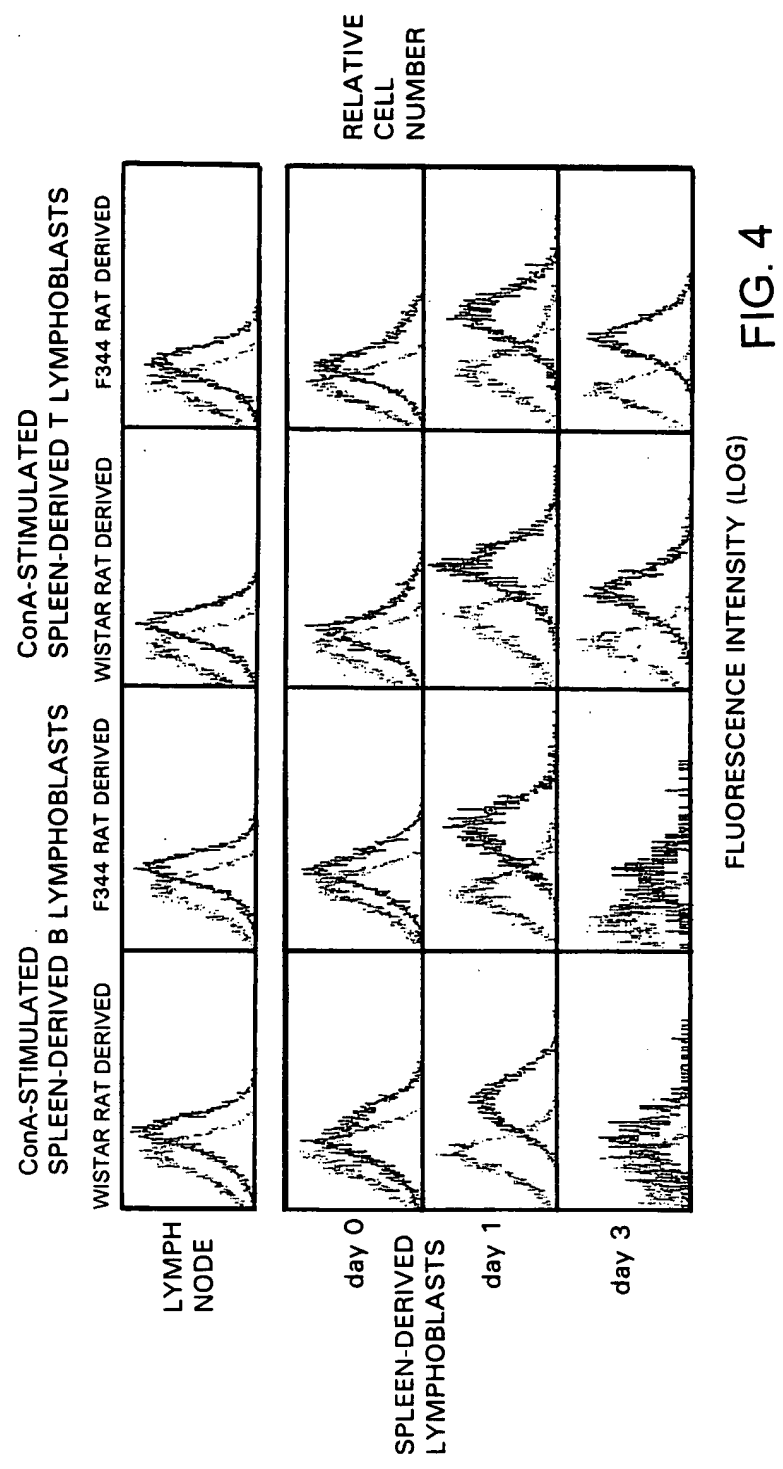


FIG. 4

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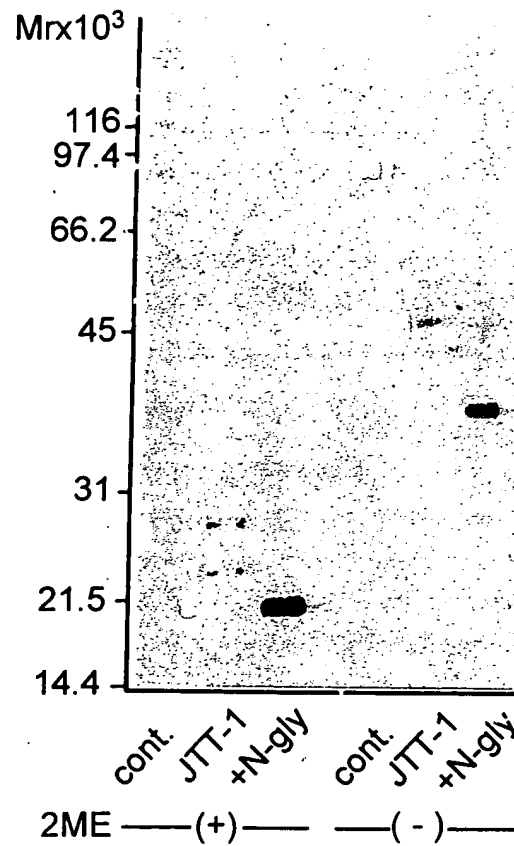


FIG. 5



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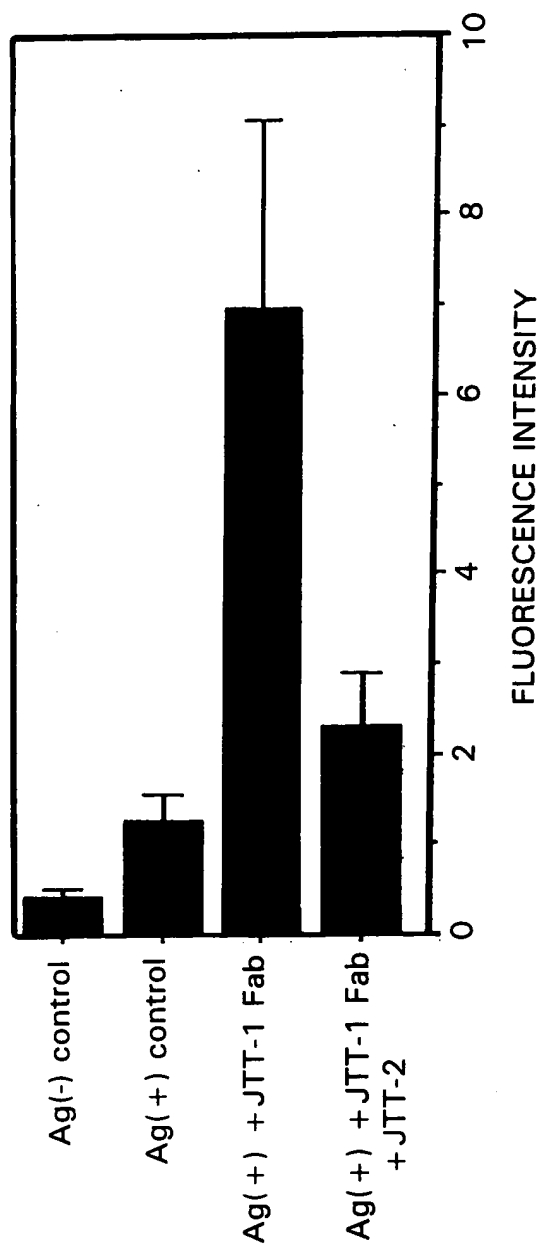


FIG. 7



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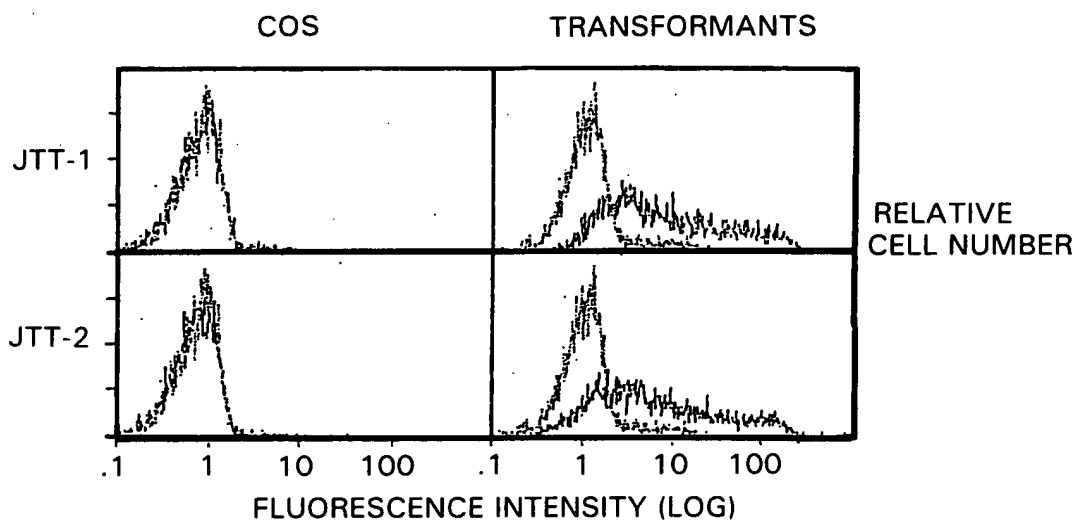


FIG. 8

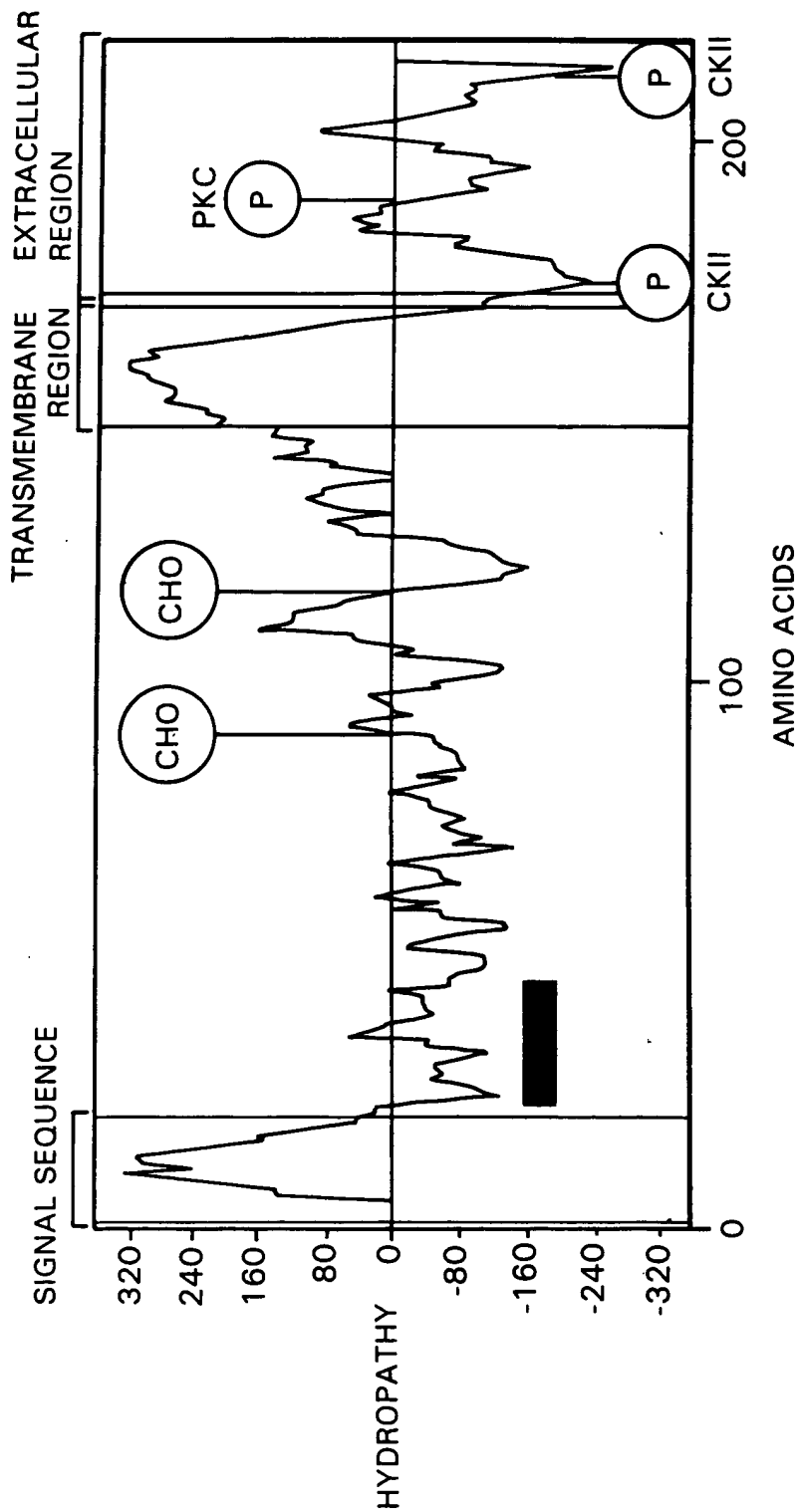


FIG. 9



human	M	K	S	G	L	W	Y	F	F	L	F	C	L	R	I	K	V	L	T	G	E	I	N	G	S	A	N	Y	E	M	F	I	F	H	N	G	G	V	Q	I	L	C	K	Y	P	P	E	T	V	Q	Q	50	
rat	M	K	P	Y	F	S	C	V	F	V	F	C	F	L	I	K	L	L	T	G	E	E	L	N	D	L	A	N	H	R	M	F	S	F	H	D	G	G	V	Q	I	S	C	N	Y	P	E	T	V	Q	Q	50	
rat mutant	M	K	P	Y	F	S	C	V	F	V	F	C	F	L	I	K	L	L	T	G	E	E	L	N	D	L	A	N	H	R	M	F	S	F	H	D	G	G	V	Q	I	S	C	N	Y	P	E	T	V	Q	Q	50	
mouse	M	K	P	Y	F	S	C	H	V	F	V	F	C	F	L	I	R	L	L	T	G	E	I	N	G	S	A	D	H	R	M	F	S	F	H	N	G	G	V	Q	I	S	C	K	Y	P	E	T	V	Q	Q	50	
consensus	M	K	P	Y	F	.	.	V	F	V	F	F	C	F	L	I	K	L	L	T	G	E	.	N	.	A	N	H	R	M	F	S	F	H	.	G	G	V	Q	I	S	C	.	Y	P	E	T	V	Q	Q	50		
human	F	K	M	Q	L	L	K	G	G	Q	I	L	C	D	L	T	K	T	K	G	S	G	N	T	V	S	I	K	S	L	K	F	C	H	S	Q	L	S	N	N	S	V	S	F	F	L	Y	N	L	D	100		
rat	L	K	M	Q	L	L	F	K	D	R	E	V	L	C	D	L	T	K	T	K	G	S	G	N	T	V	S	I	K	N	P	M	S	C	P	Y	Q	L	S	N	N	S	V	S	F	F	L	D	N	A	D	100	
rat mutant	L	K	M	Q	L	L	F	K	D	R	E	V	L	C	D	L	T	K	T	K	G	S	G	N	T	V	S	I	K	N	P	M	S	C	P	Y	Q	L	S	N	N	S	V	S	F	F	L	D	N	A	D	100	
mouse	L	K	M	R	L	L	F	R	E	R	E	V	L	C	E	L	T	K	T	K	G	S	G	N	A	V	S	I	K	N	P	M	L	C	L	Y	H	L	S	N	N	S	V	S	F	F	L	N	N	P	D	100	
consensus	L	K	M	Q	L	L	F	K	.	R	E	V	L	C	D	L	T	K	T	K	G	S	G	N	T	V	S	I	K	N	P	M	.	C	.	Y	Q	L	S	N	N	S	V	S	F	F	L	N	.	D	100		
human	H	S	H	A	N	Y	Y	F	L	C	S	L	S	I	F	D	P	P	P	P	F	Q	-	V	T	L	T	G	G	Y	L	H	I	Y	E	S	Q	L	C	C	Q	L	K	F	W	L	P	I	G	C	A	A	149
rat	S	S	Q	G	S	Y	F	L	C	S	S	L	S	I	F	D	P	P	P	P	F	Q	E	K	N	L	S	G	G	Y	L	L	I	Y	E	S	Q	L	C	C	Q	L	K	L	W	L	P	V	G	C	A	A	150
rat mutant	S	S	Q	G	S	Y	F	L	C	S	S	L	S	I	F	D	P	P	P	P	F	Q	E	K	N	L	S	G	G	Y	L	L	I	Y	E	S	Q	L	C	C	Q	L	K	L	W	L	P	V	G	C	A	A	150
mouse	S	S	Q	G	S	Y	Y	F	C	S	S	L	S	I	F	D	P	P	P	P	F	Q	E	R	N	L	S	G	G	Y	L	H	I	Y	E	S	Q	L	C	C	Q	L	K	L	W	L	P	V	G	L	P	A	150
consensus	S	S	Q	G	S	Y	.	.	C	S	S	L	S	I	F	D	P	P	P	P	F	Q	E	.	N	L	S	G	G	Y	L	.	I	Y	E	S	Q	L	C	C	Q	L	K	L	W	L	P	V	G	C	A	A	150
human	F	V	V	V	C	I	L	G	C	I	I	L	I	C	W	L	T	K	K	K	Y	S	S	S	V	H	D	P	N	S	E	Y	M	F	M	R	A	V	N	T	A	K	K	S	R	L	T	D	V	T	L	199	
rat	F	V	A	A	L	L	F	G	C	I	I	F	I	V	W	F	A	K	K	K	Y	S	S	S	V	H	D	P	N	S	E	Y	M	F	M	R	A	V	N	T	A	K	K	S	R	L	A	G	M	T	S	200	
rat mutant	F	V	A	A	L	L	F	G	C	I	I	F	I	V	W	F	A	K	K	K	Y	S	S	S	V	H	D	P	N	S	E	Y	M	F	M	R	A	V	N	T	A	K	K	S	R	L	A	G	T	A	P	200	
mouse	F	V	V	V	L	L	F	G	C	I	I	L	I	I	W	F	S	K	K	K	Y	G	S	S	V	H	D	P	N	S	E	Y	M	F	M	R	A	V	N	T	A	K	K	S	R	L	A	G	V	T	S	200	
consensus	F	V	.	.	L	L	F	G	C	I	I	.	I	.	W	F	.	K	K	K	Y	.	S	S	V	H	D	P	N	S	E	Y	M	F	M	R	A	V	N	T	A	K	K	S	R	L	A	G	.	T	.	200	
human	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	199				
rat	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	200					
rat mutant	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	200				
mouse	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	200				
consensus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	216				

FIG. 10

JTT1	M	-	-	-	-	-	-	K S G L	L	-	-	W	-	Y P F L	F C L R	I K V L	T G E I N G	S A N Y E M F I	F H	34	
CD28	M	-	L	-	-	-	-	R L L L A	-	-	-	-	-	L N L F	- P S	I I Q V	T G N K I L V	K Q S P M L V A	Y D	33	
CTLA4	M	A C L G	F Q R H K	A Q L N	L A A R T W	P C T L	L F F L L F	I P V F	C K A M H V	A Q P A V V	L A S S									50	
consensus	M	-	L	-	-	-	-	L	L A	-	-	W	-	L	L F	L	I V	Q	A		50
JTT1	NG	G V Q I	L C K Y	-	P D I V	Q Q F K	M Q L L	K G G Q I L	-	-	-	C D L T	K T	K G S G N T	V S I K	78					
CD28	NAV	- N L S C	K Y	-	S Y N L	F S R E F R	A S L H	K G L D S A	V E V	-	-	C V V Y	G N	Y S Q Q L Q	V Y S K	81					
CTLA4	R G I A	S F V C E Y	-	A S P G	K A T E V R	V T V L	R Q A D S Q	V T E V	C A A	-	-	T Y M T	G N E L T F L	98							
consensus	NG	..	C K Y	..	P	..	E F R	..	L L K G	D S	V	-	C	..	T Y	..	G N	V	..	K	100
JTT1	S L K F	C H S Q L S	N N S V	S F F L	Y N L	D H S H	A N Y Y F F	C N L S	I F D P P P P	F	-	-	K V T L T G	G	126						
CD28	T G F N	C D G K L G	N E S V	T F Y L	Q Q L	L Y V N	Q T D I Y F F	C K I E	V M Y P P P P	Y Y	-	-	L D N E K S N G T	131							
CTLA4	D D S I	C T G T S	G N Q V	N L T I	Q Q L	R A M D	T G L Y I I	C K V E	L M Y P P P P	Y Y	-	-	L G I G N G T	147							
consensus	..	C	G	L S	N N S V	F	L Q N L	C	K	E	M Y P P P P	Y	..	N G T	150						
JTT1	Y L H I	Y E S Q L C	C Q L K F	-	-	-	-	-	-	-	-	-	-	-	167						
CD28	I I H V	K G K H L C	P S P L F	P G P S K	P F W V	L V V V G G	V L A C Y S L L V T	V A F I	I F W V R S	181											
CTLA4	Q I Y V	I D P E P C	P D S D F	-	-	-	L L W I	L A A V S S	G L F F Y S F L L T	-	A V S L S K M L K	191									
consensus	I H V	..	L C	P	..	F	..	V	..	L	..	Y S	L	..	K	200					
JTT1	K Y S	S S V H D P N	G E Y M F M	R A V N	T A K K S R	-	-	-	-	-	-	-	-	-	199						
CD28	K R S	-	-	R L L H	S D Y M N M	T P R R R	P G P T	R K H Y Q P	Y A P P	R D F A A Y R S	220										
CTLA4	K R S	-	-	P L T T	G V Y V K M	P P T E	P E	-	C E K Q F Q P	Y	-	-	-	-	F I P I N	223					
consensus	K R S	-	-	L	..	G	Y M	..	K	..	Q P	Y	D F	..	-	-	242		

FIG. 11

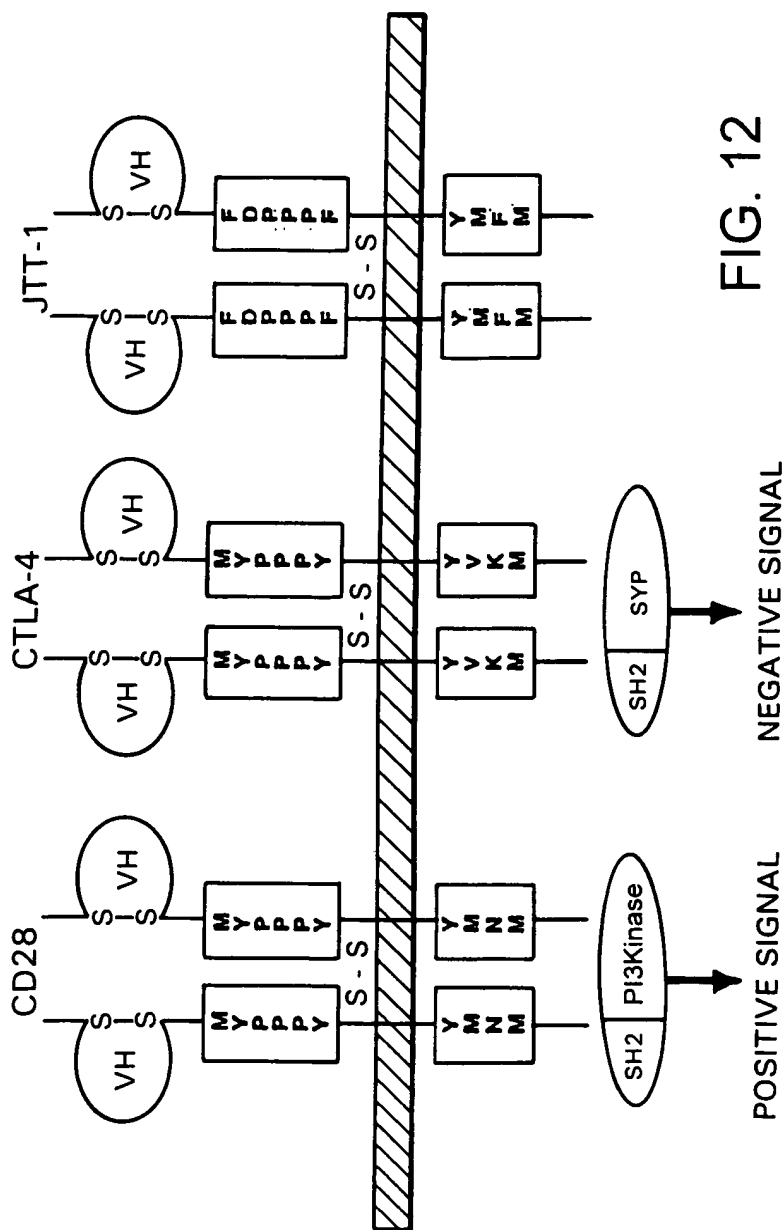


FIG. 12

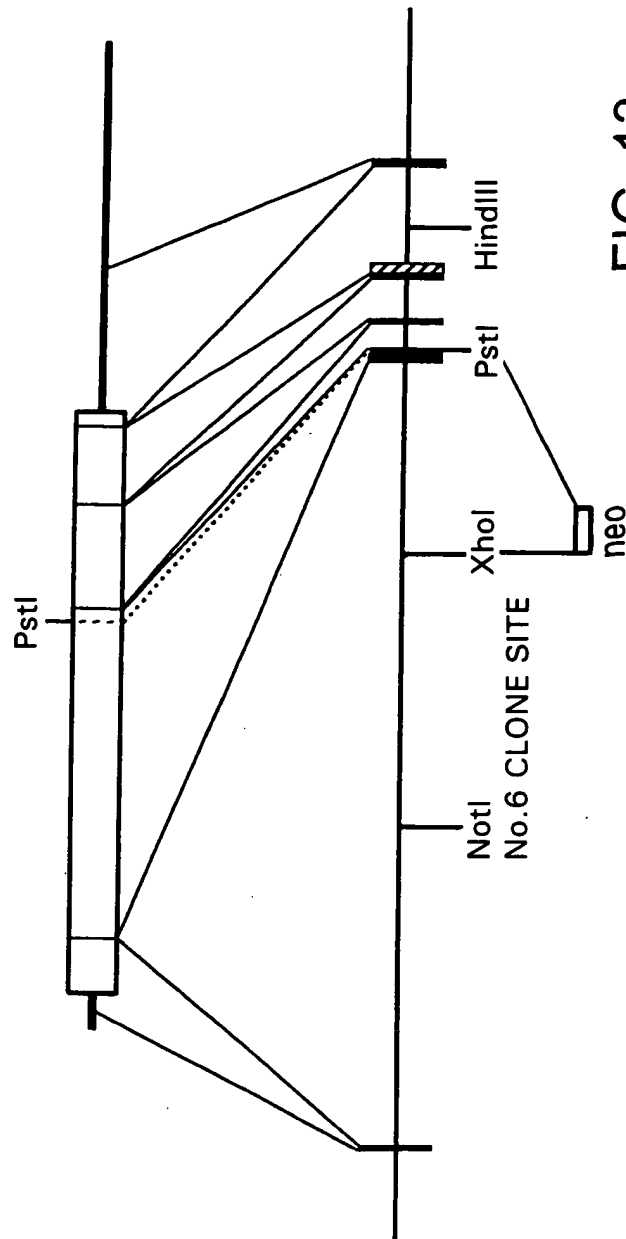


FIG. 13



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rat	50	
rat mutant	50	
consensus	50	
rat	100	
rat mutant	100	
consensus	100	
rat	150	
rat mutant	150	
consensus	150	
rat	200	
rat mutant	200	
consensus	200	
rat	200	
rat mutant	216	
consensus	216	

FIG. 14



AMOUNT OF
UPTAKE OF
[³H] THYMIDINE
(DPM)

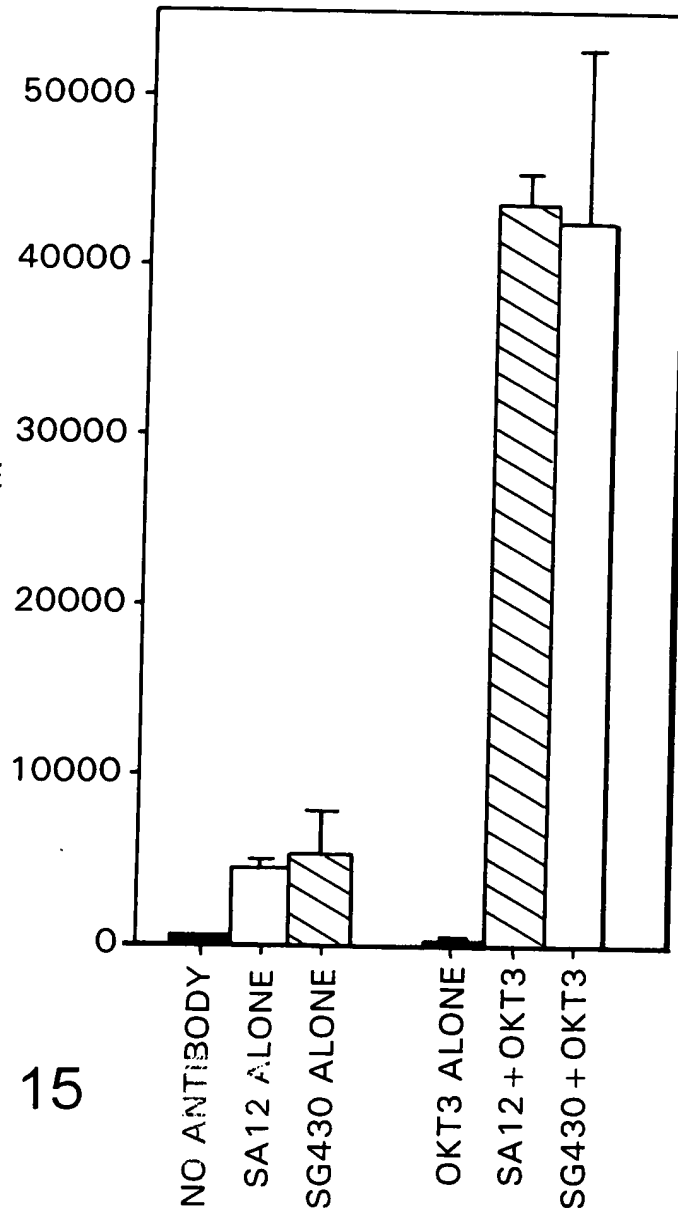


FIG. 15

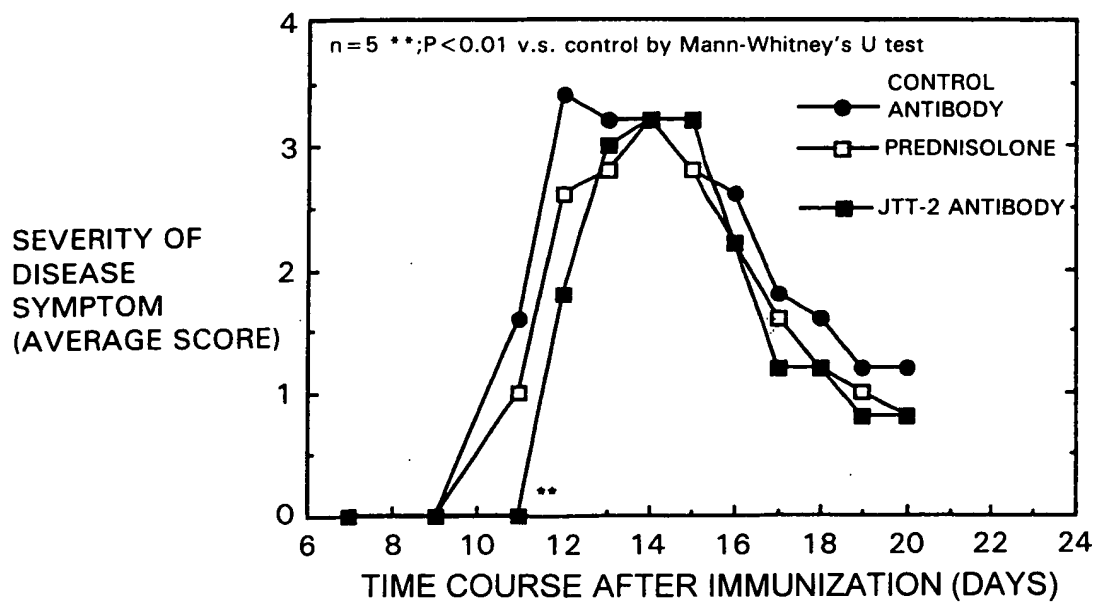
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FIG. 16

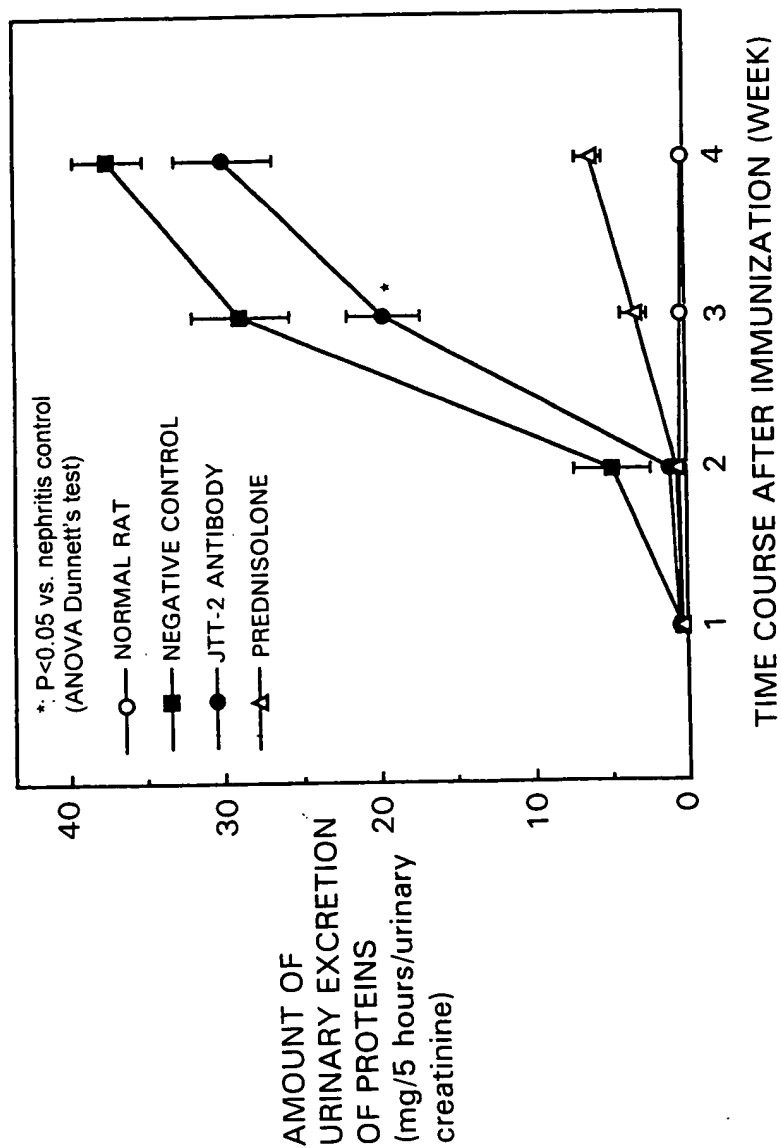
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FIG. 17



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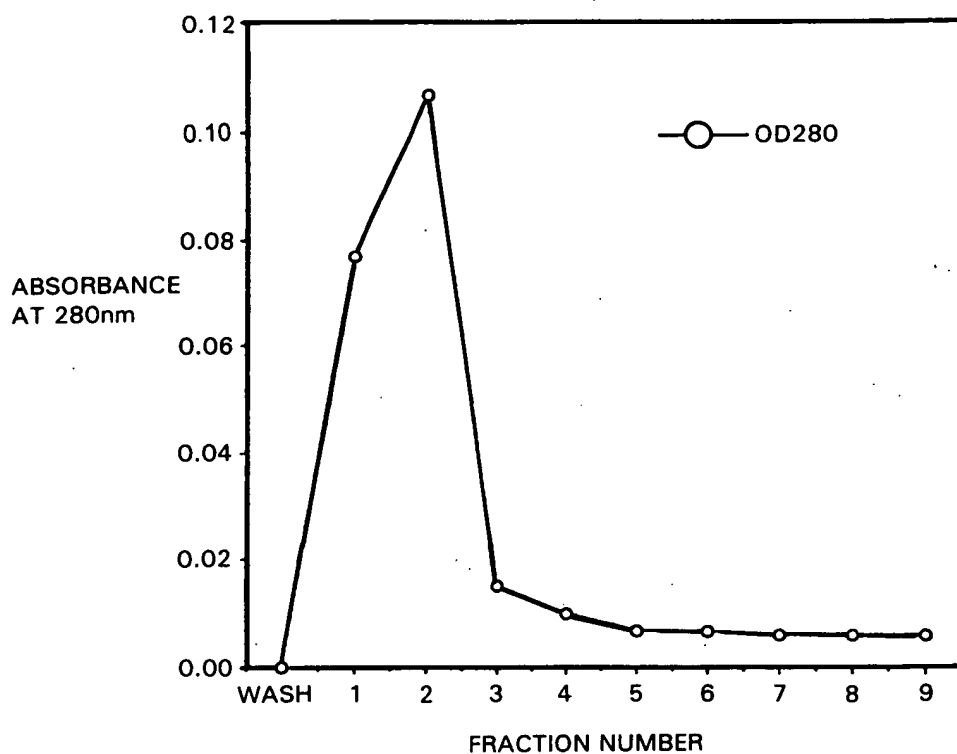


FIG. 18

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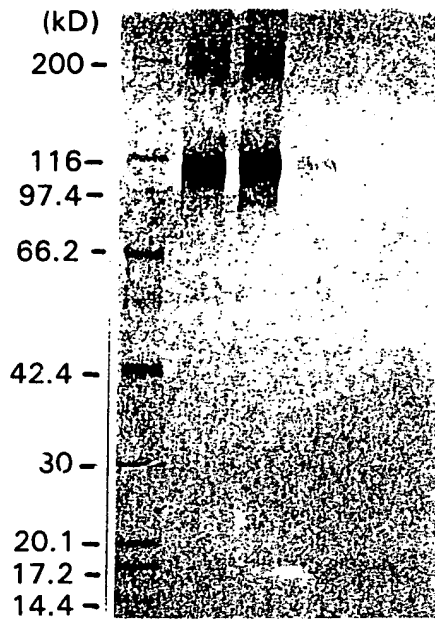


FIG. 19

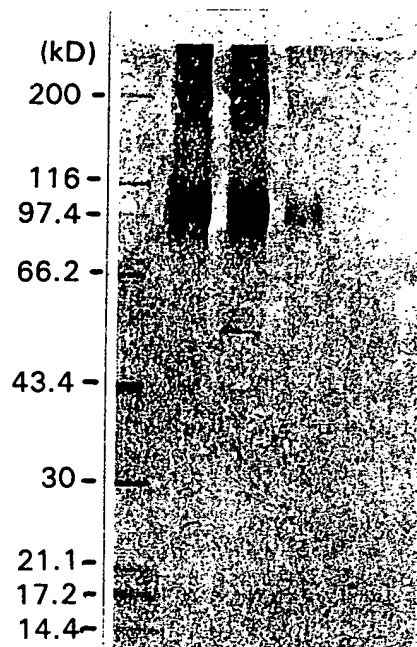


FIG. 21



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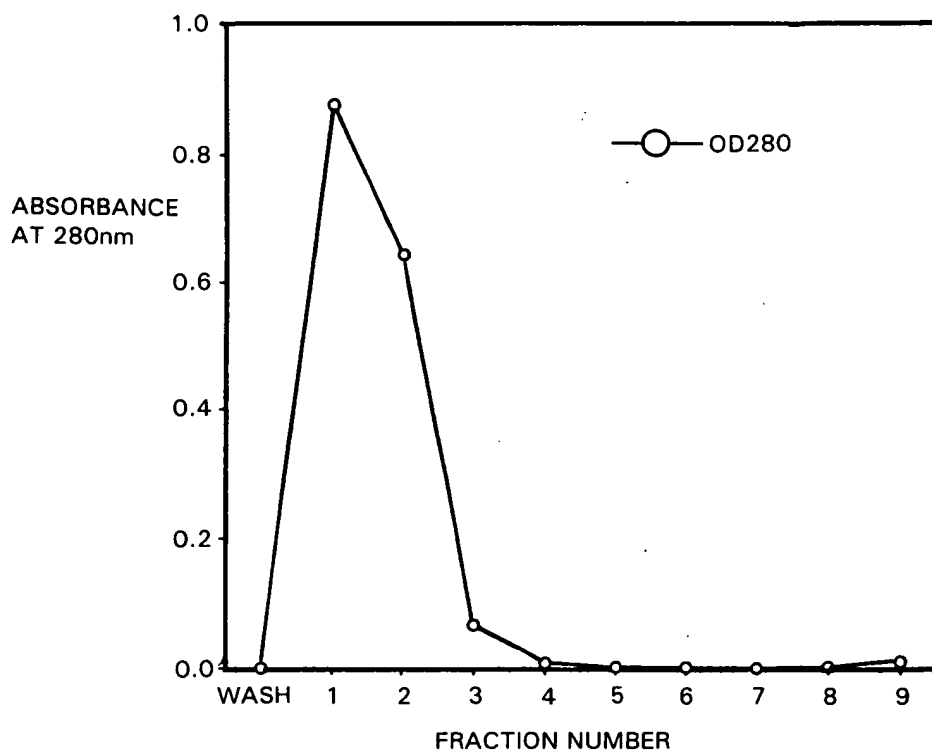
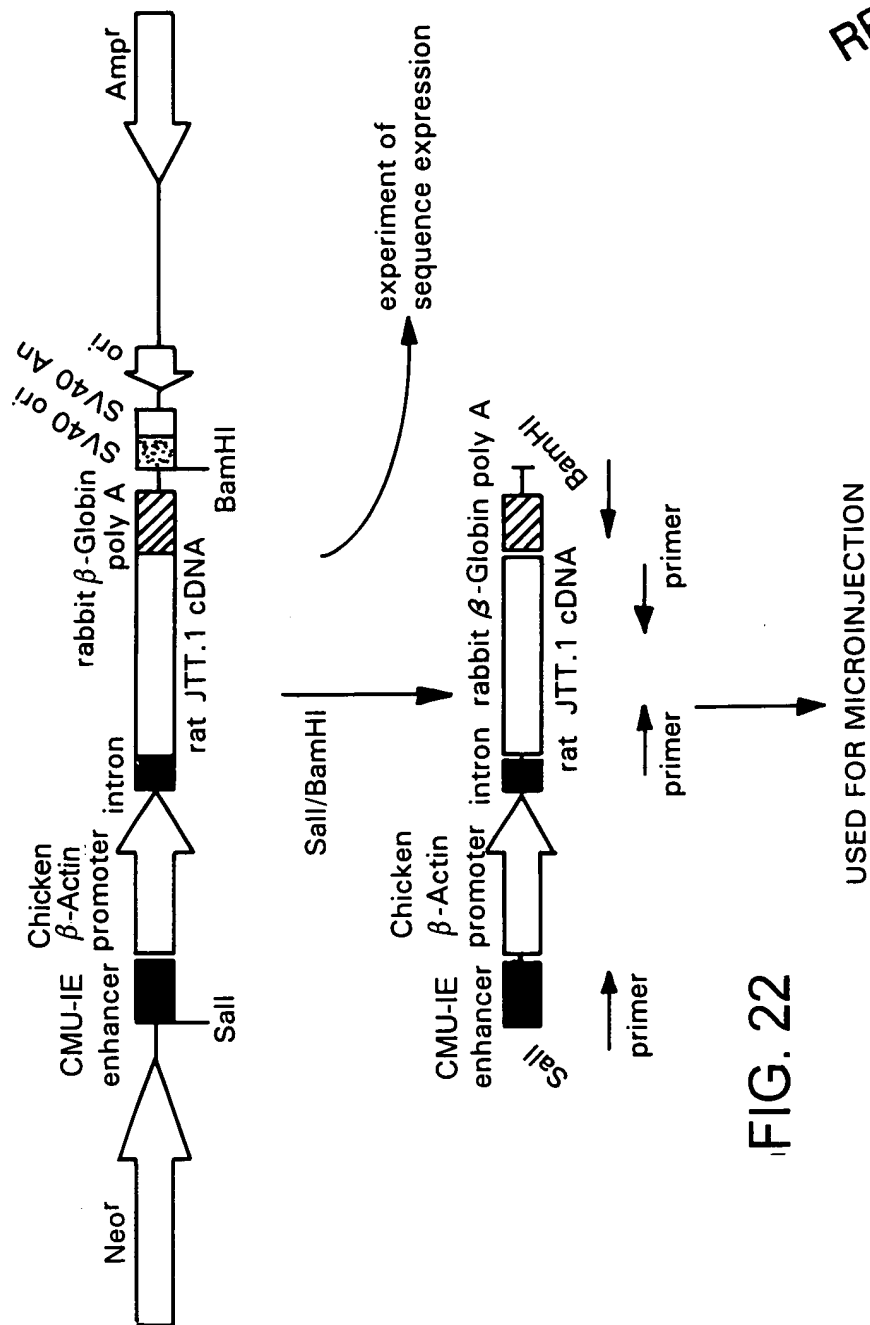


FIG. 20

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FIG. 6A

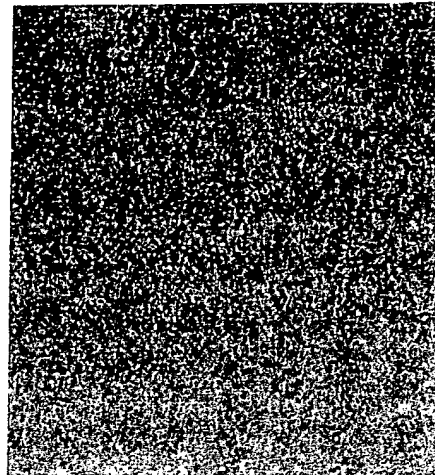


FIG. 6B

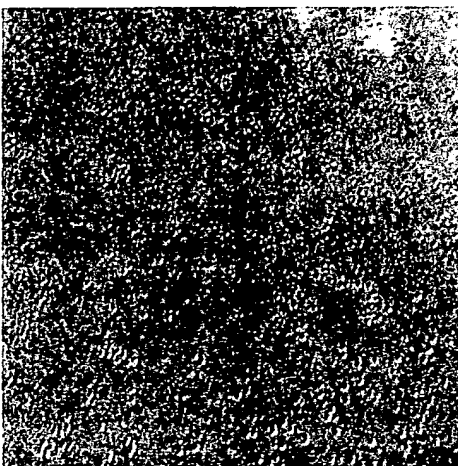


FIG. 6C

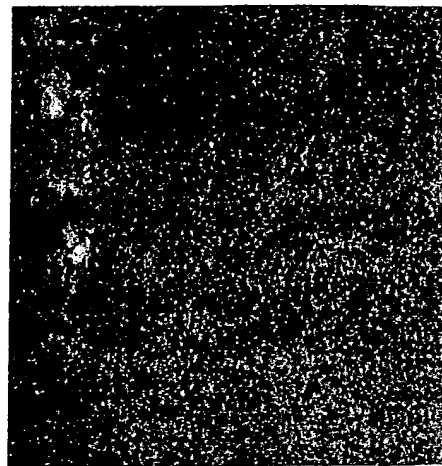


FIG. 6D